Treatment of patients with metastatic melanoma using lymphocytes transduced with an interleukin-2 (K-2) gene following the administration of a nonmyeloablative but lymphocyte-depleting regimen

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Non-Technical Abstract:

This study will be performed in patients who have metastatic melanoma. The main purpose of this research study is to determine whether special tumor fighting cells that we take from patients' blood or tumors, introduce an Interleukin-2 (IL-2) gene and grow in the laboratory, and then give back to the patient, will improve the ability to fight the patients' cancer when we suppress their immune system from attacking these special tumor fighting cells. The secondary objective of this study is to determine the survival of infused cells that have been retrovirally transduced with an IL-2 gene.

Initially patients will have cells harvested either through leukopheresis or a biopsy of their tumor. The best tumor fighting cells will be chosen to be grown in the laboratory. During the procedure to grow the cells, a piece of genetic material, called an IL-2 gene, will be introduced into the cells using the process of retroviral transduction. The retrovirus is made from a virus that has been inactivated or changed in a way that prevents it from reproducing and causing any type of illness. It serves only as a vehicle to deliver the IL-2 gene into the cells. The IL-2 gene will make the IL-2 protein, an agent that has been approved by the FDA for the treatment of metastatic melanoma. IL-2 is known to be a growth factor for the tumor fighting T-cells of the immune system. It has been shown in the laboratory to prolong the survival of the tumor fighting cells without having to give extra IL-2, which can cause side effects when given to patients.

Once the cells are grown in the laboratory and the IL-2 gene inserted, patients will be given chemotherapy, (cyclophosphamide and fludarabine) for seven days to suppress the immune system, On the eighth day, if they have a special blood type known as HLA-A201, they will be given two injections of a melanoma peptide, gp 100:209-217(210M), emulsified in an adjuvant, Montanide ISA-51, in an effort to increase the immune response. These injections will be repeated every other day for a total of three times. On the eighth day, all patients will be given the cells intravenously or intra-arterially, depending on the patients' tumor location and distribution of disease. Patients will be given appropriate medications to treat the side effects of this treatment regimen and to prevent infection secondary to the immune suppression caused by the chemotherapy.

Patients will return to NIH after four to six weeks to have their tumor(s) evaluated. If there is shrinkage of their tumor(s), the cell infusion will be repeated without additional chemotherapy. If there is no response, patients will receive the full treatment again, followed by intravenous IL-2, every eight hours beginning on the day of cell infusion for up to five days. In patients who are responding, up to three retreatment courses may be given.